Remarks

This is responsive to the official action of, March 14, 2003. The Examiner is requested to reconsider the rejections and allow all claims.

The Examiner has rejected Claims 1, 3-4, and 17 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification to enable one skilled in the art. The rejection has apparently been made on the basis that the specification does not disclose that p53as and p53 bind to the same p53 DNA binding sequence "AGGCATGCCT/AGGCATGCCT". With due respect to the Examiner, sufficient disclosure is absolutely clear. The Examiner's attention is called to page 9, lines 8-13 "...electrophoretic motility shift assays were performed using a ^{32}P-labeled double stranded oligonucleotide probe corresponding to the p53 binding sequence shown in Table 2. As shown in Fig. 2, p53as protein translated in vitro gave a strong signal representing a shift from free probe (dark signal at bottom of figure) to a higher molecular weight complex composed of protein and the labeled probe. **The p53as protein bound specifically to the p53 binding sequence..."** (emphasis added). The Examiner's attention is further called to the last paragraph of the text of the specification that says "Table 2. shows p53 DNA Binding Sequences used for assay of p53as protein binding activity." A reference to Table 2. shows the above binding sequence and Table 2 clearly says: "p53 binding sequence AGGCATGCCT/AGGCATGCCT" . There can be no other interpretation than that the sequence "AGGCATGCCT/AGGCATGCCT" binds to both p53 and p53as. The rejection is improper and should be withdrawn.

The Examiner has newly rejected claims under 35 U.S.C. (?112), first paragraph on the ground that the specification does not contain a written description sufficient to conclude that the Applicant had possession of the claimed invention at the time of filing. The rejection is not completely clear in that it is not stated with respect to the claims rejected. Claims 15-16 and 19 are mentioned by the Examiner in the discussion of the rejection and it will therefore be assumed that the rejection applies only to those claims.

The rejection of Claims 15-16 seems based upon the Examiner's argument that the claims are drawn to a plasmid containing a p53as gene sequence encoding the peptide of SEQ ID No. 1 or a portion thereof. The rejection of Claim 19 seems based upon the Examiner's argument that the claims are drawn to a viral vector containing a p53as gene sequence encoding the peptide of SEQ ID No. 1 or a portion thereof, which peptide will raise an antibody response. The Examiner has taken the position that this means that a peptide of essentially any length down to a few peptides is encompassed without sufficient description.

It is the Applicants' position that more than enough description is provided since the possible sequences are specifically taught and one skilled in the art can easily determine whether the particular sequence raises an antibody response without undue experimentation. There are only 18 amino acids in the peptide in question. It is a relatively simple matter to truncate the peptide from either or both ends and test the truncated peptide to determine whether it raises an antibody response. With only 18 starting amino acids, there would seem to be no more than about ten possibilities for a

"portion" that will raise an antibody response. It is generally believed that a peptide sequence must be at least 8 or 9 amino acids long before an antibody response is possible. In the case that an eight amino acid sequence could raise such a response, which is unlikely, there are only 55 possible sequences within SEQ ID No.1. There are only 36 possibilities in the case of sequences of ten or more. The disclosure of the base sequence (ID No. 1) with the statement that portions of the sequence that raise an antibody response are also included) is more than sufficient to support the genus.

The inventors should not be required to restrict their invention to exclude reasonable modifications that are well within the purview of the skilled artisan. These claims are not indefinite.

The rejection should be reversed.

Claims 1, 3-6, 8-11, 17 and 18 have been rejected under 35 U.S.C. 112 as containing subject matter not sufficiently described in the specification. This rejection should be reversed.

The Examiner should again be reminded that a patent specification is not intended to be a textbook including all information known and readily available to a skilled person. If such were not the case, every patent specification would be thousands of pages long rehashing known material ad nausem and hiding the nature of the improvement of the invention within unnecessarily included information.

The Examiner is making the invention much more complicated than it is. The invention is easy to understand and can be practiced to the extent of the breadth of the claims by one of even meager skill in the art in view of the teachings of the specification.

The rejection seems to be also based upon the proposition that the specification discloses only a single species of nucleic acid insufficient to support the claimed genus. This rejection should be withdrawn. The p53as genus in question is a nucleic acid sequence identical to the well known p53 sequence up to the final 50 amino acids of p53, i.e. all members of the genus have about 1140 amino acids in common with p53 with the only differences occurring within the final 50 amino acids of p53. The genus is thus different than p53 within p53's final 50 amino acids and is different than any other sequence related to p53 if the related sequence is different than p53 before the final 50 amino acids or if the related sequence has a final 50 amino acids the same as p53. These claim conditions clearly restrict and define the genus so that any person skilled in the art can understand. Further, the specification, original claims and the known state of the art at the time the application was filed make it clear that it was known that the final amino acids could be truncated from p53 to eliminate the negative regulatory domain without otherwise affecting function (Hupp, et al.). It is further made apparent in the present specification that unique antibody sites can be added at the truncated end while maintaining the function of the truncated p53. Any person skilled in the art can accomplish that task. There is no ambiguity, indefiniteness or lack of enablement. The

regulatory regions are clearly the same as the well known regulatory regions of p53, except that p53as is not controlled by the negative regulatory domain of p53.

The Examiner has again rejected Claim 16 under 35 U.S.C. 102 as being anticipated by Arai, et al.

As has already been stated numerous times during prosecution of this application, p53-M8 is not the same as p53as. p53-M8 has a Phe at position 132, and p53 and p53as have a Cys at position 132. **The sequences of p53-M8 and p53as are not the same! As previously discussed in detail, by the Attorney for the Applicants and by a declaration by one of the Applicants who is of extraordinary skill in the art, neither are the functions!**

With due respect to the Examiner, the Arai, et al., reference "**does not**" teach the plasmid claimed in claim 16. It has always been the intent of the claim that the p53as gene sequence of claim 16 be a functional p53as sequence, e.g. as set forth in claim 1. Claim 16 has thus been amended to depend from claim 1 thus clearly requiring that the sequence be functional and not merely a dismembered non-functional sequence for no purpose. The rejection should be withdrawn.

Claims 1, 3-4, and 17 have been rejected by the Examiner as being obvious over Han, et al., in view of Sambrook, et al., Hupp, et al. and Funk, et al. This rejection should be withdrawn. The rejection is a classic hindsight rejection where elements of the invention taught in the application are segregated, an attempt is made to find a reference each segregated element, the references are combined in hindsight to reconstruct the

invention, and finally justification is sought for their combination after the combination is already made. In using this hindsight method, the Examiner has found it necessary to look for four different references to support at least four different hindsight segregated elements.

The Examiner recognizes that Han, et al., does not teach incorporation of a full p53as sequence into a plasmid , virus or any other vector and comes to the conclusion that there is a suggestion to look for such incorporation merely from the statement in Han, et al., that "more precise biochemical and biological characterization of AS-p53 protein along with R-p53 protein appear to be critical in future studies of p53 function in normal cells and oncogenesis." It must be kept in mind that they are literally thousands of ways one might proceed with "more precise biochemical and biological characterization." Since Han, et al., did not actually form any proteins at all, formation of proteins based upon the disclosure of Han, et al., with respect to p53as was speculative. Whether or not the sequence contained inhibitors that prevented transcription or translation was not known, disclosed or suggested by Han, et al. Zeroing in on incorporation of a complete p53as cDNA sequence into a plasmid as a way to proceed with "biochemical and biological characterization" without any other such suggestion in Han, et al., is classic impermissible hindsight.

Sambrook, et al., does not cure this critical defect. Contrary to the Examiner's assertion, Sambrook, et al., is not concerned with DNA transcription and resulting RNA translation to make protein but is concerned only with DNA replication. **Sambrook, et**

al., is concerned with plasmid DNA replication not translation and therefore hardly addresses the "biochemical and biological characterization" suggestion made in Han, et al. Even if Sambrook, et al., had made such a general suggestion with respect to plasmids, Sambrook, et al., would not have be looked to except as a result of a hindsight search. One would not even have known whether the p53as alternatively spliced cDNA could be transcribed and then translated to form protein until it was tried. Obvious to try (even if it were present) would not be obviousness.

Hupp, et al., does nothing to cure these critical defects. There is nothing at all suggested in Hupp, et al., that would make it obvious to incorporate a p53as cDNA into a plasmid. Hupp, et al., appears not to be concerned with plasmids or any other vector.

The mere teaching of a DNA binding site by Funk similarly does not cure the critical defects described above.

This rejection is based upon an improper combination of references and even if the combination were proper, it would not disclose or suggest any embodiment of the presently claimed invention.

Claims 5-6, 8-11, and 18 have been rejected under 35 U.S.C. 103 as being obvious over Han, et al., in view of Lee, et al. This rejection is improper and should be withdrawn. Regardless of the Examiner's assertion to the contrary, the Applicants remain of the opinion that all claims are patentable over the above cited references for the reasons of record.

The Examiner recognizes that Han, et al., does not teach incorporation of a full p53as sequence into a plasmid , virus or any other vector and comes to the conclusion that there is a suggestion to look for such incorporation merely from the statement in Han, et al., that "more precise biochemical and biological characterization of AS-p53 protein along with R-p53 protein appear to be critical in future studies of p53 function in normal cells and oncogenesis." It must be kept in mind that they are literally thousands of ways one might proceed with "more precise biochemical and biological characterization." Since Han, et al., did not actually form any proteins at all, formation of proteins based upon the disclosure of Han, et al., with respect to p53as was speculative. Whether or not the sequence contained inhibitors that prevented transcription or translation was not known, disclosed or suggested by Han, et al. Zeroing in on incorporation of a complete p53as cDNA sequence into a plasmid as a way to proceed with "biochemical and biological characterization" without any other such suggestion in Han, et al., is classic impermissible hindsight. The extension to incorporation of a full p53as sequence into a virus by combination with Lee, et al., is even farther afield. Lee, et al., suggests nothing at all concerning p53as and is directed to incorporation of entirely different sequences into viruses for purposes unrelated to the function of p53as. Lee, et al., clearly does not cure the critical defect of Han, et al., related to lack of disclosure or suggestion for incorporation of a full p53as sequence into a plasmid, let alone into a virus. Viruses are discussed for no purpose in Han, et al. The purposes of Han, et al., and Lee, et al., are clearly different and have different functions and there is no reason to

combine them except on the basis of hindsight and even then the presently claimed invention is not suggested.

Claim 19 has been rejected under 35 U.S.C. 103 as being obvious over Arai, et al., in view of Lee, et al., and Sambrook, et al. Arai, et al., does not disclose or suggest the presently claimed sequence alone or within any vector, for reasons previously discussed, i.e. the Arai, et al., sequence and function is different than the presently claimed sequence and function. Neither Lee, et al., nor Sambrook, et al., suggest anything at all concerning any sequence remotely related to that presently claimed. The combination of these references therefore clearly cannot and does not suggest any of the present claims. The rejection is improper and should be withdrawn.

In view of the foregoing amendments and remarks, it is clear that all claims are now in condition for allowance, which action is courteously requested.

Respectfully submitted,

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